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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460



**OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES**

**OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361**

MEMORANDUM

Date: December 18, 2008

SUBJECT: 4-Chlorophenoxyacetic acid: Update of 3 mutagenicity executive summaries based on the March 12, 2003 TRED

PC Code: 019401

Decision No.: 404055

Petition No.: None

Risk Assessment Type: None

TXR No.: 0055046

MRID No.: see table below

DP Barcode: D359967

Registration No.: 8906-1

Regulatory Action: None

Case No.: None

CAS No.: 122-88-3

40 CFR: None

Ver. Apr. 08

FROM: Marion Copley, DVM, DABT
 Science Information Management Branch
 Health Effects Division (7509P)

Marion Copley 12/18/08

THROUGH: Nancy McCarroll, BS
 Toxicology and Epidemiology Branch
 Health Effects Division (7509P)

*[Signature] 12/18/08
 For Nancy McCarroll*

TO: Tony Kish (RM 22)
 Registration Division (7505P)

I. CONCLUSIONS

Attached are updated executive summaries for 3 mutagenicity studies with 4-chlorophenoxyacetic acid (4CPA). These updates are based on the March 12, 2003 HED Risk Assessment for the Tolerance Reassessment Eligibility Document (TRED). They do not change any results or conclusions. All 3 studies remain classified as acceptable(guideline) and satisfy their respective guideline requirements.

II. MRID SUMMARY TABLE

Study Type	MRID	Comments
84-2 Mutagenicity - gene mutation	41837002	Updated executive summary (root TXR # 0009417)
84-2 Mutagenicity - cytogenetics	41837003	Updated executive summary (root TXR # 0009417)
84-2 Mutagenicity - gene mutation	41837004	Updated executive summary (root TXR # 0009417)

4-Chlorophenoxyacetic acid/019401

In vitro Bacterial Gene Mutation Assay (1990) / Page 1 of 1
OPPTS 870.5100/ OECD 471/ DACO 4.5.4**EPA Reviewer:** Marion Copley, DVM, DABT**SIMB, Health Effects Division (7509P)****EPA Secondary Reviewer:** Nancy McCarroll, BS**TEB, Health Effects Division (7509P)****Signature:** Marion Copley**Date:** 12/18/88**Signature:** Nancy McCarroll**Date:** 12/18/88

Template version 02/06

TXR#: 0055046**DATA EVALUATION RECORD – supplemental**

See TXR # 0009417 for original DER

STUDY TYPE: *In vitro Bacterial Gene Mutation Salmonella typhimurium/* mammalian activation gene mutation assay; OPPTS 870.5100 [§84-2]; OECD 471.**PC CODE:** 019401**DP BARCODE:** D359967**TEST MATERIAL (PURITY):** 4-Chlorophenoxyacetic acid (99% a.i., lot no. not reported)**SYNONYMS:** 2-CPA**CITATION:** Lawlor, T. (1990) Mutagenicity Test on 4-Chlorophenoxyacetic Acid in the Salmonella/Mammalian-Microsome Reverse Mutation Assay (Ames Test) with a Confirmatory Assay. Hazleton Laboratories America, Inc., Kensington, MD. Study Number 12447-0-401R, December 24, 1990, MRID 41837002. Unpublished.**SPONSOR:** Beatrice/Hunt-Wesson, Inc., Fullerton, CA**EXECUTIVE SUMMARY:**

In two independently performed reverse gene mutation assays (MRID 41837002), strains TA 98, TA 100, TA 1535, TA 1537 and TA 1538 of *S. typhimurium* were exposed to 4-chlorophenoxyacetic Acid (4-CPA) (99% a.i., lot no. not reported) in dimethyl sulfoxide (DMSO) at concentrations ranging from 100 to 5000 µg/plate in the presence and absence of mammalian metabolic activation (S9).

The test was negative up to cytotoxic doses of 5000 µg/plate with no activation (-S9), and up to doses of 5000 µg/plate with activation (+S9) where no cytotoxicity was seen.

This study is classified as **acceptable(guideline)** and satisfies the guideline requirement for the requirement for Test Guideline OPPTS 870.5100; OECD 471 for in vitro mutagenicity (bacterial reverse gene mutation) data.

COMMENTS:

This supplemental DER only updates the executive summary based on the March 12, 2003 HED Risk Assessment for the Tolerance Reassessment Eligibility Document (TRED). It does not change any results or conclusions.

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4-Chlorophenoxyacetic acid/019401

In vivo Mammalian Cytogenetics - Micronucleus Assay (1991) / Page 1 of 1
OPPTS 870.5395 / OECD 474 DACO 4.5.7EPA Reviewer: Marion Copley, DVM, DABT

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Signature: Marion CopleyDate: 12/18/08Signature: Nancy McCarrollDate: 12/17/07

Template version 02/06

TXR#: 0055046**DATA EVALUATION RECORD – supplemental**

See TXR # 0009417 for original DER

STUDY TYPE: *In Vivo* Mammalian Cytogenetics - Erythrocyte Micronucleus assay in mice;
OPPTS 870.5395 [§84-2]; OECD 474.**PC CODE:** 019401**DP BARCODE:** D359967**TEST MATERIAL (PURITY):** 4-Chlorophenoxyacetic acid (99% a.i., lot no. not reported)**SYNONYMS:** 2-CPA**CITATION:** Murli, H. (1991) Mutagenicity test on 4-chlorophenoxyacetic acid in vivo micronucleus assay. Hazleton Washington, Inc., Kensington, MD. Study number 12447-0-455PO, February 7, 1991. MRID 41837003. Unpublished.**SPONSOR:** Beatrice/Hunt-Wesson, Inc., Fullerton, CA**EXECUTIVE SUMMARY:**

In an ICR mouse bone marrow micronucleus assay (MRID 41837003), 5/sex/group were treated by gavage with 4-chlorophenoxyacetic acid (99% a.i., lot no. not reported) at doses of 0, 0, 450, 900 or 1800 mg/kg-bw. Bone marrow cells were harvested at 24, 48 and 72 hours post-treatment.

There were signs of toxicity, languidness and prostration, and most animals died within 24 hours at 1800 mg/kg during the study. Hematopoiesis was adversely affected at 1800 mg/kg. There were 5000 polychromatic erythrocytes and < 5 micronucleated polychromatic erythrocytes (MPE) per group with no dose response. 4-CPA was tested at an adequate dose based on mortality. The positive control induced the appropriate response. **There was no significant increase in the frequency of micronucleated polychromatic erythrocytes in bone marrow after any treatment time.**

This study is classified as **acceptable(guideline)** and satisfies the guideline requirement for Test Guideline OPPTS 870.5395; OECD 474 for in vivo cytogenetic mutagenicity data.

COMMENTS:

This supplemental DER only updates the executive summary based on the March 12, 2003 HED Risk Assessment for the Tolerance Reassessment Eligibility Document (TRED). It does not change any results or conclusions.

4-Chlorophenoxyacetic acid/019401

OPPT 870.5300/ OECD 476 DACO 4.5.5

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Signature: Marion CopleyDate: 12/18/08Signature: [Signature] For Nancy McCarrollDate: 12/13/08

Template version 02/06

TXR#: 0055046**DATA EVALUATION RECORD – supplemental**

See TXR # 0009417 for original DER

STUDY TYPE: *In Vitro* Mammalian Cells in Culture Gene Mutation assay in mouse lymphoma cells; OPPTS 870.5300 [§84-2]; OECD 476.**PC CODE**: 019401**DP BARCODE**: D359967**TEST MATERIAL (PURITY)**: 4-Chlorophenoxyacetic acid (99% a.i., lot no. not reported)**SYNONYMS**: 2-CPA**CITATION**: Young, R., M. Cifone. (1991) Mutagenicity test on 4-chlorophenoxyacetic acid in the L5178Y TK+/- mouse lymphoma forward mutation assay with independent repeat. Hazleton Laboratories America, Inc., Kensington, MD. Study Number 12447-0-431, March 5, 1991. MRID 41837004. Unpublished.**SPONSOR**: Beatrice/Hunt-Wesson, Inc., Fullerton, CA**EXECUTIVE SUMMARY**:

4-CPA (99% a.i., lot no. not reported) was evaluated for the potential to induce forward mutations at the TK+/- locus in L5178Y TK+/- cells in two independently performed trials.

Without S9 activation, 4-CPA was not mutagenic at doses of 100, 500, 1000, 1600, 2000, 2500, 3000, 3500, or 4000 µg/mL; higher levels (5000 µg/mL) were severely cytotoxic. In the presence of S9 activation at 10, 50, 100, 250, 300, 750, 1000, 1300, 1600 or 2000 µg/mL (cytotoxic at doses of 1300 µg/mL and higher), non-dose related increases in mutation frequency (MF) were obtained in both trials. Although there was a tendency for elevated MFs at doses ranging from 300 to 1600 µg/mL +S9, doubling of the MF over concurrent controls was only seen at 600 µg/mL (Trial 1) and 1000 µg/mL (Trial 2). The evidence suggesting a mutagenic response, was however, insufficient to conclude that 4-CPA was positive. **The test material was not mutagenic in this in vitro mammalian cell assay.**

This study is classified as **acceptable(guideline)** and satisfies the guideline requirement for Test Guideline OPPTS 870.5300, OECD 476 for in vitro mutagenicity (mammalian forward gene mutation) data.

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4-Chlorophenoxyacetic acid/019401

In vitro Mammalian Cell Gene Mutation Assay (1991) / Page 2 of 2

OPPT 870.5300/ OECD 476 DACO 4.5.5

COMMENTS:

This supplemental DER only updates the executive summary based on the March 12, 2003 HED Risk Assessment for the Tolerance Reassessment Eligibility Document (TRED). It does not change any results or conclusions.



13544

R164736

Chemical Name: 4-Chlorophenoxyacetic acid

PC Code: 019401

HED File Code:

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